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TRANSMITTAL FORM

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First Named Inventor	LONG, William F. et al.
Art Unit	2621
Examiner Name	
Attorney Docket Number	15186-41US KD:lf

ENCLOSURES *(Check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☑ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
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- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
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  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) (please Identify below):

Remarks

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Printed name	Kent Daniels		
Date	March 14, 2005	Reg. No.	44,206

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	**LONG, William F. et al.**
Serial No.:	**10/624,902**
Filed:	**July 23, 2003**
Title:	**METHOD AND APPARATUS FOR SELECTING REGIONS OF INTEREST IN OPTICAL IMAGING**
Agent of Record:	**Kent Daniels** **Tel.: (613) 780-8673**

BY REGISTERED MAIL

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Sir:

Enclosed herewith for filing against the above-identified application, is the required certified copy of the priority application in this matter, i.e. Patent Application No. PCT/IB2002/04697, as filed November 11, 2002.

Respectfully submitted,

LONG, William F. et al.

Date: March 14, 2005

By: _____

Kent Daniels, Reg. No. 44,206
(Docket No.: 15186-41US KD:lf)

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PATENT COOPERATION TREATY (PCT)
TRAITÉ DE COOPÉRATION EN MATIÈRE DE BREVETS (PCT)

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International Application No. / Demande internationale n° PCT / IB 02 / 04697

International Filing Date / Date du dépôt international 11 NOVEMBER 2002 (11. 11. 02)

Geneva/Genève, 21 NOVEMBER 2002 (21. 11. 02)

International Bureau of the World Intellectual Property Organization (WIPO)

Bureau International de l'Organisation Mondiale de la Propriété Intellectuelle (OMPI)

J.-L. Baron
Head, PCT Receiving Office Section
Chef de la section "office récepteur du PCT"

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PCT REQUEST 15186-41PCTP

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0	For receiving Office use only	
0-1	International Application No.	PCT / IB 0 2 / 0 4 6 9 7
0-2	International Filing Date	1 1 NOVEMBER 2002 (11. 11. 02)
0-3	Name of receiving Office and "PCT International Application"	INTERNATIONAL BUREAU OF WIPO PCT International Application
0-4	Form - PCT/RO/101 PCT Request	
0-4-1	Prepared using	PCT-EASY Version 2.92 (updated 01.10.2002)
0-5	Petition	
	The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	International Bureau of the World Intellectual Property Organization (RO/IB)
0-7	Applicant's or agent's file reference	15186-41PCTP
I	Title of invention	METHOD AND APPARATUS FOR SELECTING REGIONS OF INTEREST IN OPTICAL IMAGING
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PCT REQUEST

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V	Designation of States	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE BG CH&LI CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH&LI CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
V-5	**Precautionary Designation Statement** In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	**Exclusion(s) from precautionary designations**	NONE
VI	**Priority claim**	NONE
VII-1	**International Searching Authority Chosen**	European Patent Office (EPO) (ISA/EP)

PCT REQUEST 15186-41PCTP

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VIII	Declarations	Number of declarations	
VIII-1	Declaration as to the identity of the inventor	-	
VIII-2	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	-	
VIII-3	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	-	
VIII-4	Declaration of inventorship (only for the purposes of the designation of the United States of America)	-	
VIII-5	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	-	
IX	**Check list**	number of sheets	electronic file(s) attached
IX-1	Request (including declaration sheets)	6	-
IX-2	Description	7	-
IX-3	Claims	4	-
IX-4	Abstract	1	EZABST00.TXT
IX-5	Drawings	2	-
IX-7	TOTAL	20	
	Accompanying items	paper document(s) attached	electronic file(s) attached
IX-8	Fee calculation sheet	✓	-
IX-17	PCT-EASY diskette	-	Diskette
IX-19	**Figure of the drawings which should accompany the abstract**	2	
IX-20	**Language of filing of the international application**	English	
X-1	**Signature of applicant, agent or common representative**		
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X-1-2	Name of signatory	ANGLEHART, James	
X-1-3	Capacity	Patent Agent and Partner of the firm	

FOR RECEIVING OFFICE USE ONLY

10-1	**Date of actual receipt of the purported international application**	11 NOVEMBER 2002	11.11.02
10-2	**Drawings:**		
10-2-1	Received		
10-2-2	Not received		
10-3	**Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application**		
10-4	**Date of timely receipt of the required corrections under PCT Article 11(2)**		
10-5	**International Searching Authority**	ISA/EP	

PCT REQUEST 15186-41PCTP

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10-6	Transmittal of search copy delayed until search fee is paid	

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11-1	Date of receipt of the record copy by the International Bureau	

METHOD AND APPARATUS FOR SELECTING REGIONS OF INTEREST IN OPTICAL IMAGING

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This is the first application filed for the present invention.

TECHNICAL FIELD

[0002] The invention relates to the field of optical imaging and more specifically to the field of selecting regions of interest in a subject for optical imaging.

BACKGROUND OF THE INVENTION

[0003] Optical imaging has evolved to become a useful diagnostic tool. Various system designs have been developed to accommodate imaging of various parts of the human body. For example, Hillman *et al*. Phys. Med. Biol, 46 (2001)1117-1130 describes an arrangement for acquiring optical signals from a forearm; and Pogue *et al*. Opt. Express 1 (1997) 391-403 describes a system for breast imaging. Optical imaging systems have also been developed for small mammals with a view of providing a research tool that can image changes in the anatomy and the physiology of the mammals and that can also provide information on the biodistribution molecules such as chromophores and fluorophores. An example of an optical imaging system for small mammals has been described in patent application WO 0137195.

[0004] Diagnosis as well as anatomical/physiological and pharmacokinetics studies rely on time course protocols to reveal temporal changes within a subject with respect to predetermined characteristics. Thus, a good imaging tool should be able to reliably and reproducibly produce images

of the same region of interest in a subject over time. In this respect accurate and reproducible positioning of the subject relative to the imaging optics is very important.

[0005] While the above mentioned optical imaging systems permit the repositioning of a subject in more or less the same position over several imaging sessions, they lack a positioning system that is reliable and precise. Thus there is a need for improved systems and methods for selecting regions of interest in a subject and reproducibly image the selected regions over time.

SUMMARY OF THE INVENTION

[0006] The present invention provides a system and method for selecting regions of interest (ROIs) in a subject such as a mammal and for reproducibly positioning the subject to image the same ROIs over time.

[0007] In one aspect of the invention there is provided a method for positioning a small mammal such as a mouse for optical imaging in which a digital image of the mammal is obtained and used to define a ROI by placing the mammal in the field of view of a camera. The ROI is then registered with an optical imaging system and the mammal is positioned relative to the imaging system in accordance with the coordinates of the ROI.

[0008] In an embodiment of the method, the ROI is selected by determining the contour of the ROI on an computer displayed image of a surface comprising the ROI.

[0009] In yet another aspect, a second digital image may be obtained to determine a plane at which the imaging system is focused for acquiring optical data when using an

optical system in which light is propagated through air and wherein the optical signal is collected using lenses.

[0010] In yet another embodiment of the method, fiducial marks are inscribed on the subject and can be used as a reference for reproducibly positioned the subject and select the same ROI over time.

[0011] The invention also provides a system for positioning a subject comprising a mammal supporting means, a camera for imaging a surface of the mammal comprising a ROI, storage means for storing the digital image, a display operationally linked to the storage means for displaying the stored digital image, a user interface to define the ROI, and a registering means for registering the defined ROI with an optical imaging system.

[0012]

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] Further features and advantages of the present invention will become apparent from the following detailed description, taken in combination with the appended drawings, in which:

[0014] FIG. 1 is a perspective representation of an embodiment of an optical imaging system comprising a system for positioning a mammal in accordance with the invention;

[0015] FIG. 2 is a computer display illustrating an embodiment of the selection of a region of interest;

[0016] FIG. 3 is a computer display illustrating the selection of a plane of optical data acquisition according to an embodiment of the invention.

[0017] It will be noted that throughout the appended drawings, like features are identified by like reference numerals.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0018] The present invention provides a system and method for selecting regions of interest (ROIs) for optical imaging in a subject such as a mammal and for reproducibly positioning the subject to image the same ROIs over time.

[0019] In accordance with one embodiment of the invention, a system for positioning a mammal or part thereof for optical imaging of a ROI of the mammal is provided, which allows the user to select a ROI of the mammal and register the selected region with an optical imaging system. This greatly facilitates manipulation of the mammal with a view of acquiring precise and reproducible optical images. In addition, the system in accordance with the invention permits the programming of the optical imaging system for automatic optical signal acquisition of the desired ROI. Furthermore, the coordinates of the ROI may be stored electronically for future retrieval and advantageously allowing the ROI to be repeatedly imaged over time, with a high degree of reproducibility. This characteristic enables time course experiments to be carried out on mammals by, for example, enabling pharmacokinetics studies, assessment of tumor growth and the like.

[0020] FIG. 1 illustrates an embodiment of an optical imaging system comprising a system for positioning the mammal 10. In one embodiment, the system comprises a camera 12, a support 14 for the mammal, and a computer 16 operationally linked to the camera and the optical imaging system.

[0021] The mammal support is preferably a heated tray that can be moved relative to the optical imaging system. This can be achieved by providing a translation stage 18 on which the tray is mounted. In addition to the motion along the translational stage, the tray may also be moved up and down to adjust the plane of optical data acquisition. The computer may be coupled to the tray in order to provide the user with a means for remotely controlling the position of the tray.

[0022] The optical imaging system comprises a combination of mirrors 20 and lens 22 for directing the light source 23 onto the surface of the mammal, and a second set of mirror 24 and lenses 26 is provided for collecting and directing the light re-emitted from the mammal to a detector. The detector is in turn linked to the computer, where the acquired optical signals are processed for generating an image.

[0023] An embodiment of the method of the present invention is now described. First, a digital image of the surface of the mammal comprising the ROI is acquired by exposing the surface to the field of view of the camera 12. The digital image of the ROI permits the user to define the ROI and register the ROI with the optical imaging system as will be described below. Software instructions can then be used for proper positioning of the mammal relative to the optical imaging system in order to acquire the optical signals for image reconstruction. Acquisition of the image is preferably performed with the table at a predetermined position relative to the optical imaging system so as to provide an internal reference of coordinates.

[0024] Once the digital image has been acquired, the ROI may be defined by displaying the image of the surface comprising the ROI on a display screen 28 (FIG. 2). The user may then select the ROI 30 using a user interface drawing device, such as a mouse, for example. The selection of the ROI triggers the computer to digitally record the coordinates of the ROI. The coordinates may be stored in a memory for later retrieval.

[0025] The coordinates of the ROI are then used to program the optical imaging system to scan the region defined by the coordinates. This may be accomplished, for example, by programming the position of mirrors to direct the illumination beam and the optical signals re-emitted from the mammal to the appropriate location. In addition to defining the ROI, the user may also define the positions 32 within the ROI where the surface is to be illuminated by the beam of light, and the position where the optical signals re-emitted from the surface of the mammal are to be collected. Selection of illumination and detection points depends on the desired mode of optical imaging (continuous wave, time or frequency domain), the desired resolution, whether the image is topographic or tomographic and the like.

[0026] In a further embodiment, the system may also comprise a second camera 34 located on a side of the apparatus so as to provide a field of view that is substantially perpendicular to the field of view of the camera used to acquire the digital image of the surface comprising the ROI. In optical imaging systems in which the light is propagated through air (i.e. through free space optics) and wherein light re-emitted from the mammal is collected with lenses, the second camera allows the

acquisition of a digital image that can be used to determine a plane 36 of optical data acquisition within the ROI (FIG. 3). Accordingly, the image acquired by the second camera may be stored in the computer and displayed on a screen, thereby enabling the user to define a desired plane of imaging. As for the selection of the ROI, the plane of imaging may be selected using a user interface device, such as a mouse, for example.

[0027] In a preferred embodiment, the cameras are located in a positioning chamber 38 optically insulated from the chamber 40 comprising the optical components by baffle 42. In this embodiment, the tray may be moved back and forth between the optical chamber and the positioning chamber by displacement on the translation stage which spans the two compartments. This permits the user to easily manipulate the mammal in the positioning chamber without interfering with or risking disturbing the various optical components.

[0028] In another embodiment fiducial marks may be inscribed on the mammal to provide references that can be used to select the region of interest when a plurality of optical images are acquired over time so that the same region of interest is selected and registered with the optical system.

[0029] The embodiment(s) of the invention described above is(are) intended to be exemplary only. The scope of the invention is therefore intended to be limited solely by the scope of the appended claims.

I/WE CLAIM:

1. A method for positioning a mammal or part thereof for optical imaging, the method comprising:

   i) obtaining a digital image of a surface of the mammal comprising a ROI;

   ii) defining the ROI;

   iii) registering the ROI with an optical imaging system;

   iv) positioning the mammal relative to the optical imaging system to image the ROI.

2. The method as claimed in claim 1, wherein the step of obtaining a digital image comprises:

   i) positioning the mammal on a support so as to expose the surface of the mammal comprising the ROI to a field of view of a camera; and

   ii) acquiring a digital image of the exposed surface.

3. The method as claimed in claim 2, wherein the step of defining the ROI comprises:

   i) displaying the image of the surface comprising the ROI on a display;

   ii) selecting the ROI to digitally record coordinates of the ROI; and

   iii) storing the digitalized coordinates of the ROI in a computer.

4. The method as claimed in claim 3, wherein the step of registering the ROI with an optical imaging system

comprises programming the optical imaging system to acquire optical data from the ROI defined by the digitalized coordinates.

5. The method as claimed in claim 4, further comprising the step of determining a plane relative to the mammal at which the imaging system is focused for acquiring optical data.

6. The method as claimed in claim 5, wherein the step of determining a plane for image acquisition comprises:

i) obtaining a digital image of a surface of the mammal defined by a plane substantially perpendicular to the plane of the surface of the mammal comprising the ROI;

ii) defining a plane corresponding to a desired plane relative to the mammal at which the imaging system is focused for acquiring optical data;

iii) digitally recording coordinates of the defined plane;

iv) storing the coordinates of the defined plane;

v) registering the plane of image acquisition with the optical imaging system; and

vi) positioning the mammal relative to the optical imaging system to image the ROI at the defined plane of optical data acquisition.

7. The method as claimed in claim 6 wherein a plurality of images of the ROI are obtained over time and wherein the stored coordinates of the defined plane

and of the ROI are used for positioning the mammal at substantially the same position for each image.

8. The method as claimed in claim 7 wherein fiducial marks are inscribed on the surface of the mammal in the ROI to provide reference for positioning the mammal at substantially the same position for each image and for selecting substantially the same ROI.

9. A system for positioning a mammal for optical imaging, the system comprising:

i) a mammal supporting means;

ii) a camera for digitally imaging a surface of the mammal comprising a ROI;

iii) storage means for storing the digital image;

iv) a display operationally linked to the storage means for displaying the stored digital image;

v) a user interface to define the ROI; and

vi) a registering means for registering the defined ROI with an optical imaging system.

10. The system as claimed in claim 9, wherein the mammal supporting means is a tray.

11. The system as claimed in claim 10, wherein the tray is moveable relative to the optical imaging system.

12. The system as claimed in claim 10, wherein the tray is a heated tray.

13. The system as claimed in claim 12, wherein the system further comprises a second camera positioned such as

to provide a field of view substantially perpendicular to the field of view of the first camera.

14. The system as claimed in claim 13 wherein the first and second camera, the mammal supporting means, the storage means, the display, the user interface and the registering means are operationally linked to a computer.

ABSTRACT OF THE DISCLOSURE

[0030] There is provided a method and system for positioning a mammal for optical imaging in which a digital image of the mammal is obtained using a camera and a region of interest is selected using the digital image. The selected region is registered with an optical imaging system and the mammal is positioned in the imaging system to image the selected region of interest.

PCT/IB02/04697

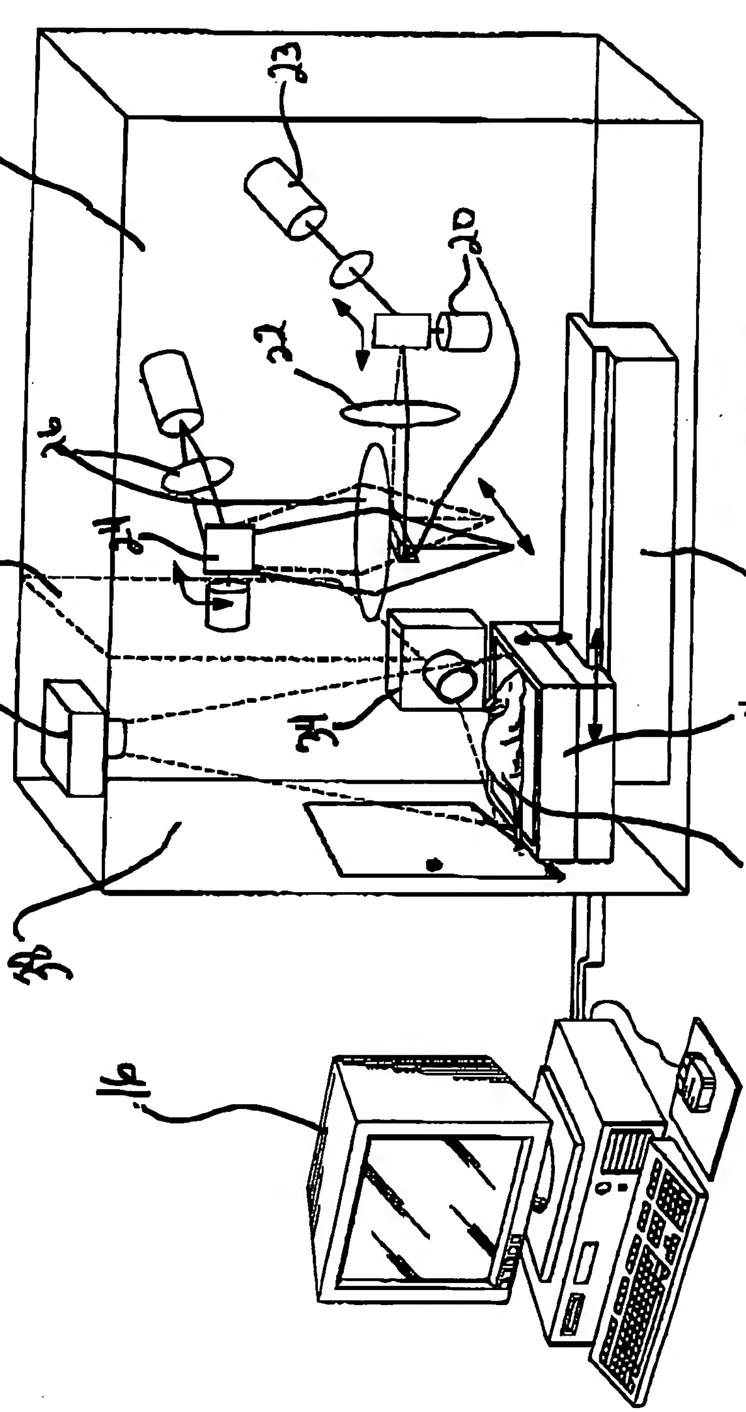

FIG. 1

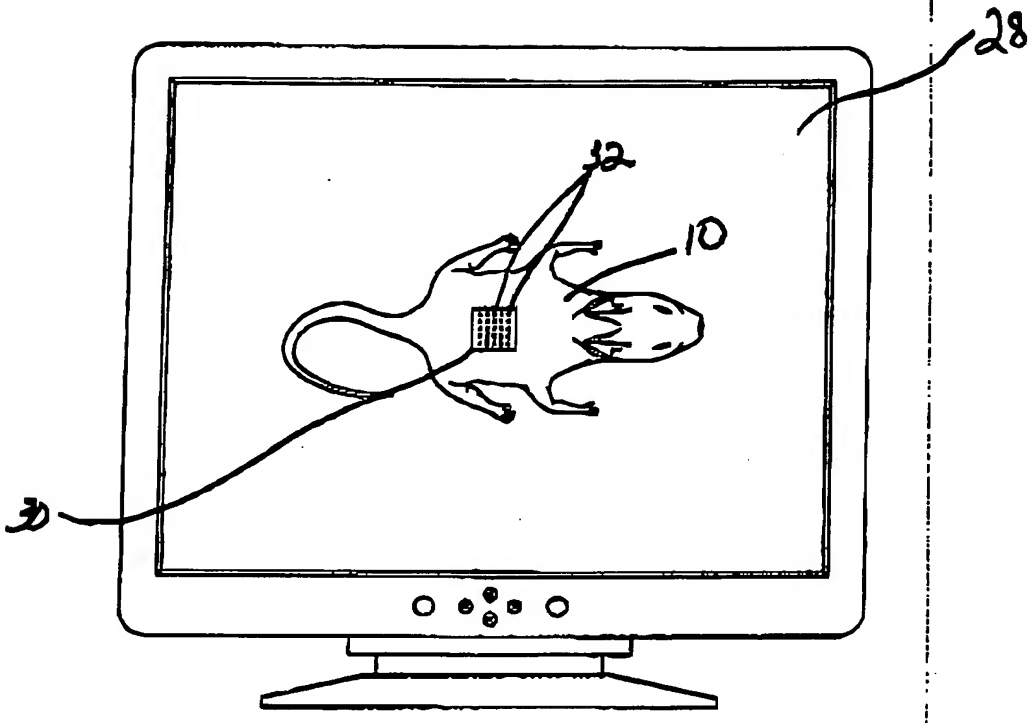

Fig. 2

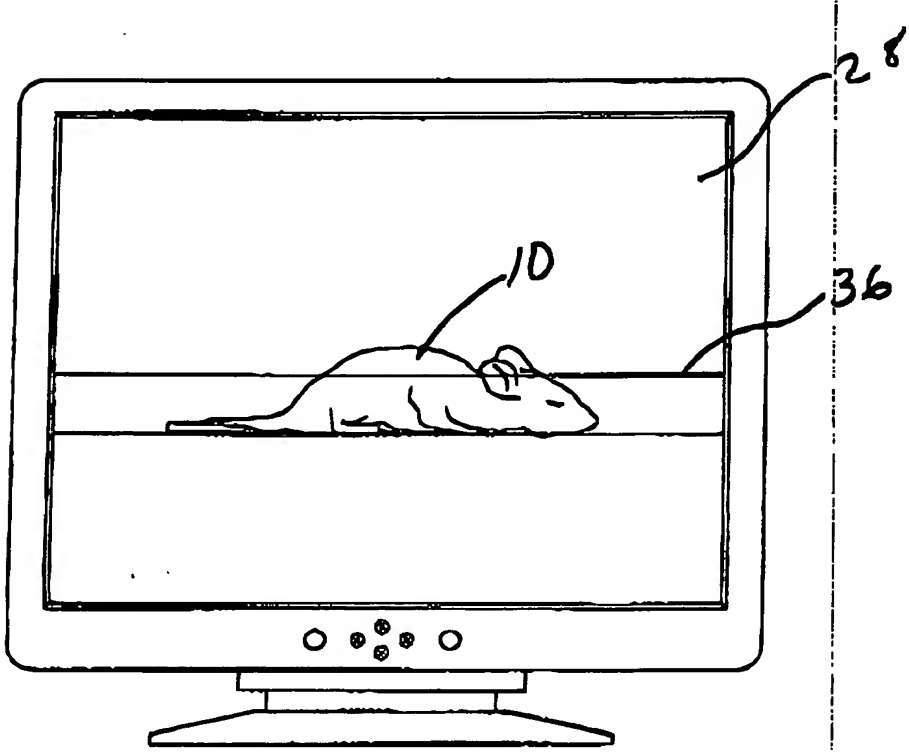

Fig. 3